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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,592	07/13/2001	Keiya Ozawa	50026/012003	6387

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EXAMINER	
AKHAVAN, RAMIN	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Applicant 8/23/04 RS

Office Action Summary	Application No.	Applicant(s)	
	09/905,592	OZAWA ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,8,10,12,14,15 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,8,10,12,14,15 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/142,305.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of an amendment, filed 05/58/2004, amending claims 5-6, 8, 10, 12, 14-15, 17, canceling claims 9, 11 and 13, and adding new claims 18-19. Claims 5-6, 8, 10, 12, 14-15 and 17-19 are pending and under consideration in this action. Any objections or rejections not repeated herein are hereby withdrawn. Where applicable, applicants' arguments will be addressed in the body of the rejections. In addition, any new grounds of rejection set forth are necessitated by material amendments to the claims, thus **this action is FINAL.**

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

1. **Claim 14, 15, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

The claims recite the term, "vector system" which confers ambiguity and indefiniteness to the claims. It is unclear how this term is to be interpreted in determining the claims' metes and bounds, because "system" implies a group of interacting, interrelated or interdependent elements forming a complex whole. The specification does not delimit this embodiment, but rather indicates that a "vector system" *includes* multiple vectors and *comprises*, a vector comprising a fusion protein and a vector comprising an exogenous gene. (e.g. Spec. p. 6, ¶ 2). The term "system", as used in the claims or in the specification, implies additional steps, processes, elements or components, which remain undefined and indefinite.

In other words, the specification only indicates that the system can have as one of its elements or components, multiple vectors, but such a teaching does not clarify, what a "system" specifically entails, thus the specification does not limit the term "vector system" to a degree. In sum, the limitation is open-ended and subjective, thus making indeterminable the claims' metes and bounds.

Claim 15 is drawn to an isolated cell according to any one of the claims "8 to 12". This range of claims includes claims that are cancelled, thus it is unclear if applicants intention is for such cancelled claims to be revived. As such the claim's metes and bounds are indeterminable.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 5-6, 8, 10, 12, 14-15 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record and as set forth herein.

The claims contain subject matter, proliferation-inducing parts of cytokine receptor domains (i.e. variants)[1] interacting with any ligand-binding domain to induce proliferation in any cell, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The claims are drawn to a genus in terms of any variant of any cytokine receptor domain that transduces a proliferation signal in any cell. Therefore, the claims

[1] The claims recite the term, "parts thereof" which is analogous in meaning to the term "variant".

are drawn to a vast number of structures each with the correlative function of inducing proliferation of any cell. Furthermore, even where the cytokine receptor is delimited to G-CSF (claim 10), the claim is still drawn to a genus of structures – "parts thereof" – with the prescribed function of inducing cell proliferation. The written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics sufficient to show applicant was in possession of the claimed genus.

The specification does not provide sufficient description for a representative number of structural properties coupled with a known or disclosed structure to function correlation. The specification provides a single example of Ba/F3 or murine mononuclear cells transformed with three variants of one type of cytokine receptor proliferation domain (i.e. G-CSF receptor). There is no other disclosure as to the vast genus of variants for proliferation domains; applicants only recite the claimed domains by functional means without any disclosure as between the limitless number of structures and the correlative function. The evidence in the art does not provide that all variants from all cytokine receptors are known and clarified with respect to the prescribed function of inducing proliferation of any cell. (See infra, under Response to Arguments; discussing Applicants' arguments in this regard).

Given the enormous breadth of the cell-proliferation cytokine receptor domain variants encompassed by the rejected claims, and given the limited description from the instant

specification of such variants, the skilled artisan would not have been able to envision a sufficient number of specific embodiments to describe the broadly claimed genus of cell-proliferation cytokine receptor domain variants. Moreover, an applicant claiming a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from other species. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.

Response to Arguments

Applicants' assertion that the written description requirement has been satisfied is not deemed persuasive. Applicants submit that the specification or the evidence in the art teach a sufficient number of species for the claimed genus of structures. With respect to the proliferation-inducing cytokine receptor domain portion (variants) of the fusion constructs, Applicants contend that the specification alone satisfies the written description requirement. (Remarks, pp. 13-14). First, applicants point out that the specification teaches that variants are domains, which impart proliferation activity to a cell. (Remarks, p. 13, bottom). However, merely correlating a claimed structure to a prescribed function does not indicate that applicants are in possession or that one of skill can envisage the claimed structures.

Next, applicants point out exemplary fusion proteins in support of their argument. (Remarks, p. 14; noting Fig. 1). However, even within the single cytokine receptor – G-CSF – single substitutions or mutations in the proliferation domain would provide a distinct structure with no evidence to suggest such a structure would have the requisite proliferative activity in any

cell. Therefore, the three embodiments do not satisfy the written description requirement, because even for a single cytokine receptor, the number of variants that can be produced would number in the thousands, merely by substituting a single amino acid residue. The number of variants would number in the tens of thousands when considering all variants for all cytokine receptors inducing proliferation of any cell.

Applicants also contend that the specification describes methods for engineering fusion constructs and that one of skill could routinely isolate a proliferation-inducing domain of a cytokine receptor without undue experimentation. The written description requirement should not be confused with the enablement requirement. Descriptions for engineering fusion constructs and methods for isolating function domains are not relevant to a written description requirement but would be relevant to an enablement requirement (i.e. teaching how to *make* an invention).

Finally, applicants cite several publications in the art as support for the assertion that the disclosed estrogen and G-CSF fusions are representative of all steroid hormone and cytokine receptors. This assertion is incorrect. None of the evidence cited clarifies a sufficient number of structures (i.e. variants) for a particular cytokine receptor. In other words, the art does not teach that any proliferation-inducing variant from the vast number of cytokine receptors can induce proliferation of any cell. Furthermore, with respect to a particular cytokine receptor, even if a handful of variants were taught, such a teaching would not be sufficient to satisfy the written description requirement for a particular cytokine receptor domain, because such a description would not provide a sufficient number of structures capable of inducing proliferation in any cell, as each particular variant can transduce a particular cell type to proliferate. (See e.g., Watowich

et al. Annu. Rev. Cell Dev. Biol. 1996; 12:91-128; p. 94, bottom; noting that certain colony stimulating factors or cytokines support proliferation in cells of specific lineages, while others may influence multiple blood cell lineages; p. 116, bottom; noting that different cytokine receptors support proliferation of distinct hematopoietic lineages). In sum, the specification and evidence in the art do not disclose a sufficient number of embodiments encompassed by the vast genus of proliferation-inducing variants of cytokine receptor domains.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 5, 6, 8, 10, 12, 15 and 17 are rejected as being anticipated by Capon et al. (US 5,837,544; see whole document; hereinafter the '544 patent).

The term "kit" is interpreted as broadly as reasonable as comprising any containment, e.g. tubes containing the vectors/cells containing or a freezer box containing said tubes as well as additional tubes/boxes containing for example a specific ligand.

The '544 patent teaches a chimeric constructs encoding a ligand-binding domain and a proliferation signaling domain (PSD), as well as vectors and cells containing said constructs. (e.g. Abstract). More particularly, the chimeric construct can comprise an inducer-responsive

clustering domain (ICD), i.e. hormone receptor domain, which upon binding the inducer or ligand will dimerize or cluster. (e.g. col. 3, ll. 33-39; See also, Fig. 1). Furthermore, the ICD domains can be eukaryotic steroid receptor molecules, including estrogen, progesterone, androgen, for example. (e.g. col. 14, last ¶). In addition, the PSD portion of the chimeric construct can be the transducing domains (i.e. proliferation domains) of the cytokine receptors, including IL-2 for example. (e.g. col. 16, last ¶ bridging to col. 17, ll. 1-19). Further, the PSD can be G-CSF. (e.g. col. 9, l. 54).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 5, 6, 8, 10, 12, 14, 15 and 17-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6-8, 10-14, 16-18 and 20 of copending Application No. 10/100,471.

The newly presented grounds of rejection based on obviousness-type double-patenting will not preclude the finality of this Action. This ground of rejection involves conflicting claims in a copending application newly discovered by the Examiner, which has inventors in common

with the instant application, and Applicants did not call attention of the Office to this application. Applicants will not be permitted to extend prosecution of the present application by reason of their inaction with regard to providing notice to the Office of conflicting claims in a copending application, the discovery of which necessitated the new grounds of rejection at this advanced state of prosecution. Indeed, with appropriate notice, these grounds of rejection clearly could have been incorporated in the prior Office Action. These circumstances are analogous to the policy of making an action final where Applicant's material amendments to the claims necessitate a new ground of rejection, since in both instances it is the applicant who caused the rejection to be applied after the case had received an action on the merits. See M.P.E.P. § 706.07(a). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are directed to biologically and patentably indistinguishable subject matter. But for some alterations in the language of the claims, the subject matter is similar in each set of claims. For example, instant base claim 1 is directed to a vector comprising a gene encoding a fusion protein, while reference base claim 1 is directed to a fusion protein comprising the same limitations of having a ligand-binding domain from a steroid receptor and a cytokine receptor domain or part thereof that imparts proliferation activity. Furthermore, reference claims 6 and 7 are further directed to vectors DNA and vectors comprising the DNA that encodes the fusion protein of reference claim 1. Thus, but for semantic changes and the order of terms such as "vector" and "fusion protein" the claims are directed to patentably indistinguishable subject matter. Additional claims are directed to cells (instant claims 6, 15, 19:

reference claims 8), kits containing said DNA constructs (instant claim 17; reference claim 20) as well as additional vectors encoding an exogenous gene (instant claims 14, 18, 19: reference claims 10-14). Therefore, the instant and reference claims are necessarily obvious over one another.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can

be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ray Akhavan/AU 1636

GERRY LEFFERS
PRIMARY EXAMINER